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Carbamate Toxicity and Protective effect of vit. A and vit. E on some biochemical aspects of male albino rats

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ABSTRACT

The effect of daily oral administration of carbamate (1/10 $L.D_{50}$) on rats for 30 successive days were studied. The male rats were divided into five groups (control, control + oil, carbamate, carbamate + vit. A and carbamate + vit. E). Each group (except control and control + oil) was daily administrated carbamate (0.012 mg/kg B.wt.). Two groups of carbamate – intoxicated animals provided with vit. A (700 mg/kg.B.wt) or vit. E (10 mg/kg.B.wt). Poisoning symptoms were recorded, e.g. unbalanse, diarrhea, have poor health and posterior limbs rigidity. Haematological parameters showed a significant decrease in red blood corpuscles (R.B.Cs), white blood corpuscles (W.B.Cs) count, Haemoglobin concentration and haematocrit value in groups treated with carbamate, and an improvement in these values was observed in groups treated with the anti-oxidants (vit. A and vit. E). Total lipids cholesterol, total proteins, albumin, glucose, LDH, AST, ALT, adrenaline and noradrenaline were measured in serum. Total proteins, total lipids, of tissues (liver, heart, muscle and kidney) were investigated.

The present study declare that, carbamate induced a significant elevetion in serum LDH, glucose. total lipids,cholesterol, AST, ALT, adrenaline and noradrenaline. On the other hand, causes a significant reduction in total proteins and albumin.

The total lipids and total proteins of the tissue were recorded highly significant decrease in the group treated with carbamate only. From another point of view, antioxidant ameliorated the effect of carbamate on tissues. So, it is clear that administration of vit. E or vit. A. reduced the effect of carbamate on biochemical alteration to various extent. The antioxidant property of vitamin A and vitamin E seem to be responsible for the observed protection against carbamate intoxication.

INTRODUCTION

The environmental pollution is one of the most serious problems that faces mankind in this century. There are many types of pollutants that interfere with our-life both directly and indirectly. Furthermore, potential future hazards to human health and wildlife can be created by residues from some long-lived pesticides, that may build up in the food chain and cause widespread contamination of the environment (El-Sebae, 1993).

More than 30,000 metric tons formulated pesticides (carbamate) were important and used annually in the density population area along the green strip of land beside the river Nile and

North Delta (El-Sebae, 1994). Some carbamates may become incorporated into fruits and vegetables from absorption through the roots (El-Sebae, *et al*., 1994).

Carbamate poisoning is a well known toxicological problem in developing countries, but well still has, even in industrialized ones, a high mortality rate and a frequent invalidating outcome (Lifshitz *et al*., 1994). Serious problems especially arise from cardiac, muscular and neural behavioral (regressive psychosis, cognitive, and percepitive alterations). Such complications, caused by direct neural cardiac and muscular damage. Carbamate inhibit the enzyme acetyl cholinesterase (ACHE) which is present in erythrocyte and plasma in man (Rana and Jaga, 1991) and in rat (Tyaniwara, 1991).

Carbamate inhibit brain and plasma cholinesterase in aves and mammals (Hunt and Hooper, 1993) and rabbits (Takahashi et. Al., 1994). Carbamates share organo-phosphates in having single pharmacological properties chiefly manifested by the inhibition of cholinesterase (ACHE) which plays a decisive part in the transmission of nerve impulses and stimulate the parasympathetic nervous system. The use of quaternary carbamates as parasympathomimetic substances was reported since 1926 (Weinstein, 1953 and Tether, 1956). Carbamates have toxic symptoms and physiological changes in different animals. Toxic effects of carbamates were noticed in frogs and birds (Mullie *et al*., 1991) and suspected cause of death in ducks (Yuningshi and Dan, 1985). They cause congenital abnormalities and death in sheep and cats (Grendon and Frost, 1994 and McCoy *et al*., 1994). Carbamates causes occupational disorders and occupational-hazards in human (Senthilselvan *et al*., 1992). They cause toxic effects on slug, (Singh *et al*., 1982; Singh and Agarwal, 1983, 1984). Goswamy *et al*. (1994) reported desperate, vomiting, mitosis and cyanosis in human.

Carbamates also cause significant changes in total serum lipids, glucose, protein levels AST, ALT, acid phosphatase and alkaline phosphatase activities in mammals (Sadek *et al*., 1989; Fayez and Kilgore, 1992 and Chevalier *et al*., 1993). They affect liver glucose 6-phosphatase and liver succinic acid dehydrogenase (Fayez and Kilgore, 1992) liver and Kidney acid phosphatase, AST and ALT activities (Kiran *et al*., 1988). In birds, there was a decrease in cholesterol, glycogen, protein, alkaline and acid phosphatase content in adrenal gland (Graham *et al*., 1981).

It is becoming increasingly recognized that free radicals play a significant role in the pathogenesis of certain diseases, drug-associated toxicity and viral infections (Reilly *et al*., 1991, Halliwell *et al*., 1992 and). Oxidations would arise from the normal production of free radicals during cellular respiration (Chakraborty *et al*., 1994). It is assumed that reduction of this oxidative damage is possible by increasing the antioxidant capacity of tissues and cells. Vitamin A and vit. E (anti-oxidants) act as detoxifying and protective agents. The vitamins also nullify the increasing effect of the pecticides (carbamate or organophosphorus). Anti-oxidants prevent cell damage from free radicals or lowers free radicals damaging effects. So vit. A and vit. E are considered as good protective materials for carbamate toxicity and tissuse

injury. The body's anti-oxidant system (liver) is an integrated one in which some components may interact to space or replace each other (Jacob, 1995).

Vitamin E is one of the natural antioxidants with low toxicity (Philips, 1977). In animals supplemental vitamin E affords also protection against various drugs, metals and chemicals that can initiate free radical formation (Bleri *et al*., 1983 and Polasek, 1997).

Also Vit. E act as a free radical scavenger or vit E is a chain breaking anti-oxidant and singlet oxygen quencher and vit. E is also thought to be an immune modulator enhancing cell mediated as well as humoral immunity (Bagchi and Puri, 1998).

The present investigation, was carried out to study the effect of the carbamate on LDH, total lipids, total proteins, Albumin, glucose, cholesterol, AST, ALT, adrenaline and noradrenaline in serum. Also, to study its effect on different vital tissues. And to illustrate the acion of vit. A . and vit. E as antidotes.

MATERIAL AND METHODS

Fifty five male adult albino rats (Rattus norvigicus), weighing from 120 to 150 gram from animal house of National organization for drug control and Research (NODCAR) were used in this work. Animals were kept in cages with proper ventilation and illumination. They were supplied with adequate standard diet and water were given *ad libitum* for one weak in the laboratory.

Animals were divided into the following groups:

Group I : Five rats were served as a control groups.

Group II : Five rats were given diet supplemeted with oil (0.01 ml) Maize oil.

Group III : Five rats were given carbamate 8-hydroxy quinaldin N-N`-dimethyl-carbamate dimethyl sulphate (1/10 LD_{50}) in dose of 0.012 mg/kg B.wt./day

Group IV : Five rats were given carbamate (1/10 $L.D_{50}$) and vitamin A (700 mg/kg/.B.wt/day).

Group V : Five rats were given carbamate (1/10 $L.D_{50}$) in addition to antioxidant (vit. E) in a dose of 18 mg/Kg B.wt/day.

All the doses were given to rats by gastric incubation daily for 30 days. During the experimental period any clinical signs of poisoning were recorded. At the end of the experiment, rats were sacrificed, blood was collected from the animals and centrifuged, other part of blood was collected on EDTA for hematological analysis. Serum was kept at –20°C till used for biochemical analyses. Rats were rapidly dissected and selected organs were taken, and weighed small pieces where put in an appropriate amount of 30% KOH for total protein determination or in concentrated sulphoric acid for total lipids estimation. Red and white blood cells were counted according to the method of Rodak (1995). Haemoglobin concentration was measured using the method of Van Kampen and Zilstra (1961). Haematocrit value was carried out by using the method of Rodak (1995).

Analysis of serum for biochemical parameters: total protein content was evaluated according to the method of Doumas (1975). Albumin was estimated according to the Doumas method (1971), serum total lipid level was determined colourimetrically by the method of Knight *et al*. (1972). Serum total cholesterol level was measured according to the method of Sidel *et al*. (1983). Serum glucose concentration was determined colourimetrically using

the method of Trinder (1969). Serum aspartate amino transferase (AST) and alanine-amino transferase (ALT) activities were assessment colourimetrically according to the method of Reitman and Frankel (1957).

Serum lactate dehydrogenase activity was measured by using LDH diagnostic kit purchased from Boehringer Manheim. Serum adrenaline and Noradrenaline concentrations were determined by radio-immuno assay kit according to the method of Stein and Black (1991).

All values are expressed as means ± standard error. The statistical comparison between control and treated group were analyzed using student "t" test according to Snedecor and Cochrane (1980).

RESULTS AND DISCUSSION

Symptoms of poisoning with carbamate included severe convulsions, tonoclonic spasms and dyspnea.

Haematological analysis:

The data illustrated in Table (1) and figure (1), indicated that 1/10 LD_{50} of carbamate induced a significant decrease ($P < 0.01$) in $R.B.C_s$ and $W.B.C_s$ count almost always throughout the experimental period. Also there was a decrease in haemoglobin concentration and haematocrit value as exhibited in table (1) and figure (1).

Haematology is a valuable tool for assessing the injuries that caused by carbamate. Blood parameters (red and white blood cells count, haemoglobin concentration and haematocrit value) form a synergistic link in all vertebrate. So they will be discussed together. The reduction in the blood parameters may be attributed to internal haemorrhage, possibly as a consequence of the toxic effect of carbamate on bone-marrow, splean and liver as reported by Reena *et al*. (1989). However, El-Sebae *et al*. (1994) suggested that the reduction in $R.B.C_s$ (Erythrocytopenia) and $W.B.C_s$ (Leucopenia) count, Hb. concentration and Hct value may be due to microcytic or hypochromic anaemia.

Erythropenia in rats treated with carbamate may arise due to depression of erythropoiesis, Leukopenia in rats following carbamate may be due to depression of leukopoiesis, alteration of cell membrane or disintegration of white blood cells, because white blood cells combat against any carbamate introduced into the blood stream. The observed leukopenia found in treated rats suggest that the immune response of rats was suppressed. These suggestions were supported by the observations of Saleh *et al*. (1998).

Serum analysis:

It is clear from table (2) and fig. (2) that animals treated with carbamate 1/10 LD_{50} (0.012 mg/kg b.wt.) had highly significant increase ($P \leq 0.01$) of serum total lipids and total cholesterol in carbomate group only. The elevation in serum total lipids and cholesterol shown in our results was also reported by Fayez and Kilgore (1992), Gupta *et al*. (1994), Zaahkouk *et al*. (1996) and Dekundy *et al*. (2000), who reported that this increase may be due to the stimulations of catecholamines which stimulate lipolysis, and due to the increase of fatty acid production.

The elevation in serum total cholestrol level that observed in the present investigation, may be attributed to the blockage of liver bile ducts causing reduction or cessation of its secretion to the duodenum. Consequently it appeared in the serum causing cholestasis. These results are in agreement with the findings reported by Hassan *et al*. (1995), Badawy (1997) and Helal *et al*. (1997).

In addition, Hassan *et al*. (1988) declared that the disruption of the formation of lipoprotein is one of the

factors leading to accumulation of cholesterol in carbamate treated rabbits. Moreover, Zaahkouk *et al*. (1996) suggested that intraperitoneal injection of carbamate compound has increased tissue lipogenesis this has been achieved through acceleration of acetyl COA which supposed by Newsholme and Leech (1985) to be the precursor of cholesterol biosynthesis. From another point of view, Ahmed. (1994) reported an alteration in total cholesterol level of serum in mammals exposed to carbamate.

The present results revealed that serum total proteins and albumin level of male rats were significantly decreased ($P < 0.01$) by treatment with carbamate when compared with control group.

Carbofuran has been reported to decrease serum protien level in hens but carbamate serum protein was not affected serum protein at any dose level in rats (Fayez and Kilgore, 1992).

As shown in table (2), rats treated with carbamate compound recorded a highly significant increase in serum glucose which may be due to increase glycogenolysis, decrease utilization of glucose by the tissue and/or increase gluconeogenesis, this agrees with the results on hens were recorded a decrease in liver glycogen level after administration of carbamate (Berberian and Enan (1987) and Anam and Metra (1995) . The same data were observed by Dekundy *et al*. (2000) indicates an enhanced rate of glycolysis due to carbamate stress.

Fayez and Kilgore (1992) and Anam and Maitra (1995) attributed the elevation of blood glucose concentration to accumulation of acetylcholine in the adrenals following, inactivation of cholinesterase by the insecticides which stimulate the release of adrenaline into the blood, adrenaline increases cell metabolism; it causes glycogenolysis in the liver and a consequent hyperglycemia as demonstrated in pesticide-exposed animals. Also, an accumulation of acetylcholine in some parts of the brain, e.g., hypothalamus, humoral factors, are released systemically which cause mobilization of peripheral glycogen stores leading to hyperglycemia (Fox and Vigro, 1986).

The present results confirm the later suggestion where a marked elevation of both adrenaline and noradrenaline was noticed after oral intake of carbamate (table 2 and fig. 3) Nakai and Ichihara, (1994) showed that the increased catecholamine (adrenaline and Noradrenaline) accompanied by decreasing in insulin level and increased blood glucose concentration.

In addition, Hassan *et al*. (1988) reported that the changes in carbohydrate metabolism (increased blood sugar level) induced by carbamate can be correlated with its effect on the activities of hepatic enzymes. Furthermore, Begum and Vijayaraghavan (1995) reported that the necessity for increasing energy by the liver in the process of detoxification may be reflected in the disturbance in both glycogenolysis and glyconeogenesis process which in turn reflect in the changes of glucose level in serum (hyperglycemia). However, the increase in serum glucose level may be induced by a decrease in endogenous insulin release due to damage of pancreatic tissue (Helal *et al*., 1997).

The ability of the liver to synthesize glycogen is enhanced during insecticide toxicity (El-Sebae *et al*. 1993). It is also evident from the presented data in table (2) and fig. (2), that lactate dehydrogenase activity exhibited a significant increase ($P < 0.01$) in case of carbamate treated group. It was also

noticed that the use of both antioxidant ameliorate this effect (table 2). LDH enzyme system plays a principal role in the glycolytic cycle in the cell for conservation of stored energy (i.e. pyrovate or lactate), this enzyme is released by injury to many different tissues (Hamdy 1993) and Lohitnavy and Sinhason (1998).

Furthermore, a highly significant incrase ($P < 0.01$) in the activity of serum AST and ALT was recorded in case of carbamate treated group, while no significant changes was noticed in all other groups as in table (2) and fig. (2). This increase may be due to the hepatic potency of carbamate resulting in destructive changes in the hepatic cells. The carbamate was administered orally and, hence, it reaches the liver first throughout the hepatic portal vein. The effect of the carbamate on the liver is in accordance with Kiran *et al*. (1988) who reported that carbamate stimulates AST and ALT of the liver *in vivo* and *in vitro*. They added that the observed stimulation of ALT activity is due to carbamate interaction with the enzyme

molecule rather than with the tissue. It also shows its hepatotoxic effect on the liver and other extrahepatic tissues.

Transaminases (AST and ALT), represent a group of enzymes that are present within the cytoplasm of the living cells. The highest concentrations of ALT are found in liver tissue; while lower concentrations exist in heart muscles and relatively small amounts present in brain, kidney and serum. AST was found to have its highest concentration in a variety of tissues including liver, kidney, brain, skeletal and cardiac muscles (Cook, 1974).

The elevation in tranaminases activity that was noticed in the present study suggests the existence of heavy drain during carbamate stress, which is known to induce elevation of serum transaminases (Kulkarni and Mehrotra 1973). From another point of view, elevation of transaminases activity in blood have been considered as indicator of tissue damage, without any specific damage of one organ. Damaged cells release transaminases into blood stream, and factors such as alteration in permeability of cell membrane, increased synthesis or decreased enzyme degradation may be involved.

However, Luckens and Phelps (1969) and Walker *et al*. (1969) recorded that the elevation in serum AST and ALT was due to degeneration and necrosis of lvier cells which was accompanied by damage of cell-walls and cytolysis, thereby pouring considerable amount of these mitochondrial enzymes in the blood stream.

It has been reported that serum ALT raised only when cells of liver parenchyma are destroyed (Varley, 1969). For this reason serum. ALT is more linked with liver disease. The

possible mechanisms involved in the evation of serum ALT may be related to tissue damage (Korstud et al., 1972).

However, Friend *et al*. (1955) reported a relationship between the degree of elevation of serum AST activity and the degree of liver necrosis. Also, Molander *et al*. (1955) found that the amount and duration of increased serum AST activity was noted to be proportional to the amount of toxin administered and to the extent of liver cell damage, since liver is the main detoxifying tissue.

Tissue analysis:

Data of total tissue protein of liver, heart, muscle and kidney indicated no significant change for all tested animals groups except that of carbamate group which revealed a significant decrease ($P < 0.05$) in liver protein and a high

significant decrease in ($P < 0.01$) in heart, muscle and kidney protein as shown in table (3). In accordance with these results, a decrease of nucleic acids and total protein of liver were recorded in birds (Saleh, 1990) and different mammals (Mekkawy *et al*., 1981; El-Sayed, 1986; El-Fiky *et al*., 1992 and Amer *et al*., 1994).

In table (4), carbamate induce a highly significant decrease ($P \leq 0.001$) of tissue total lipids in all tested organs as liver, kidney, muscle and heart tissues. Data presented in this investigation showed that carbamate compound caused a general hypercholesterolemia. Cholesterol is usually obtained in the diet but, if necessary, sufficient for normal requirement can be synthesized in the liver, intestine and other tissues, virtually all nucleated cell have the capacity to synthesize this compound, but the quantitatively important tissue is the liver (Newsholme and Leech, 1985). It is reasonable to suggest that carbamate compound has increase tissue lipogenesis probably, this has been achieved through acceleration of acetyl COA which was supposed by Newsholme and Leech (1985) to be the precursor of cholesterol biosynthesis. On the other hand, no significant changes were noticed with groups treated with antioxidant.

In conclusion it's clear that the use of antioxidant ameliorate the damage effect of cabamate not only in serum parameters, but also in different vital tissus as heart, muscle, kidney and liver. This indicate that both of vitamin A. and E. can use as antidote and also as a protective agent against the different and fetal hazards of carbamate toxicity.

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Table (1): Effect of carbamate, 1/10 LD_{50} (0.012 mg/kg b.wt) on haematological parameters.

Parameters \ Treatment		Control	Control + oil	Carbamate	Carbamate + Vit. A	Carbamate + Vit. E
R.B.C$_s$ x 10^6 cell/mm^3	Mean	7.2	6.8	4.5	6.7	6.8
	± S.E	0.4	0.3	0.3	0.3	0.2
	Probability		N.S	P < 0.01	N.S	N.S
Hb g/dl	Mean	12.5	12.0	9.5	12.2	12.1
	± S.E	0.6	0.7	0.4	0.3	0.5
	Probability		N.S	P < 0.01	N.S	N.S
Hct %	Mean	38.8	36	30	37.6	37.8
	± S.E	0.3	0.4	0.7	0.5	0.4
	Probability		N.S	P < 0.01	N.S	N.S
W.B.C$_s$ x 10^3 cell/mm^3	Mean	10.5	11.5	7.4	13.4	12.5
	± S.E	0.4	0.7	0.3	0.4	0.4
	Probability		N.S	P < 0.01	N.S	N.S

Table (2): Effect of carbamate, 1/10 LD_{50} (0.012 mg/kg b.wt on some biochemical parameters in serum of albino rats.

Parameters \ Treatment		Control	Control + Oil	Carbamate 1/10 LD_{50}	Carbamate + Vit. A	Carbamate + Vit. E
Total lipids g/dL	Mean ± S.E Probability	406.2 4.68	420 6.5 N.S	468 1019 P ≤ 0.01	426 7.83 N.S	412.0 5.4 N.S
Total Cholesterol mg/dL	Mean ± S.E Probability	113.2 3.19	108.6 2.25 N.S	131.6 3.15 P < 0.01	115 2.85 N.S	114 2.84 N.S
Total protein G/dL	Mean ± S.E Probability	7.6 0.42	7.5 0.36 N.S	6.0 0.23 P ≤ 0.01	7.0 0.69 N.S	6.8 0.40 N.S
Albumin g/dL	Mean ± S.E Probability	3.34 0.1	3.2 0.18 N.S	2.42 0.10 P < 0.01	3.68 0.13 N.S	3.43 0.17 N.S
Glucose mg/dL	Mean ± S.E Probability	111.8 4.85 N.S	116.0 2.74 N.S	165.0 6.24 P < 0.01	124.8 5.74 N.S	119 3.32 N.S
LDH	Mean ± S.E Probability	519.5 10.9	523.9 1.7 N.S	580 10.2 P < 0.01	525.01 12.9 N.S	529.1 7.3 N.S
AST (GOT) u/L	Mean ± S.E Probability	25.4 0.70	2.78 0.70 N.S	38.8 0.90 P < 0.01	24.8 0.90 N.S	28.0 0.90 N.S
ALT (GPT)	Mean ± S.E Probability	32.6 2.2	34.4 1.07 N.S	58.4 4.9 P < 0.01	36.8 1.48 N.S	34.4 338 N.S
Adrenaline ng/L	Mean ± S.E Probability	2.26 0.02	2.22 0.04 N.S	2.38 0.02 P < 0.01	2.2 0.01 N.S	2.12 0.01 N.S
Noradrenali ng/L	Mean ± S.E Probability	1.85 0.02 N.S	1.74 0.06 N.S	2.10 0.02 P < 0.01	1.71 0.01 N.S	1.78 0.02 N.S

Table (3): Effect of 1/10 LD_{50} of carbamate on tissue total proteins (mg/g tissue) of different organs in male albino rats.

Parameters \ Treatment		Control	Control + oil	Carbamate	Carbamate + Vit. A	Carbamate + Vit. E
Liver	Mean ± S.E Probability	65.5 2.5	62.2 2.9 N.S	53.4 2.7 P < 0.05	62.1 2.4 N.S	63.2 2.5 N.S
Heart	Mean ± S.E Probability	20.1 0.5	19.0 0.6 N.S	15.1 0.4 P < 0.01	18.9 0.3 N.S	18.0 0.2 N.S
Muscle	Mean ± S.E Probability	19.8 0.3	20.1 0.5 N.S	15.1 0.3 P < 0.01	18.9 0.3 N.S	18.1 0.5 N.S
Kidney	Mean ± S.E Probability	16.4 0.4	16.5 0.2 N.S	12.2 0.3 P < 0.01	15.5 0.4 N.S	16.0 0.2 N.S

Table (4): Effect of, 1/10 LD_{50} of carbamate on tissue total lipids (mg/g tissue) of different organs in male albino rats.

Parameters \ Treatment		Control	Control + oil	Carbamate	Carbamate + Vit. A	Carbamate + Vit. E
Liver	Mean ± S.E Probability	100.0 2.6	115.1 2.4 N.S	90.0 2.4 P < 0.01	96.8 2.5 N.S	97.0 2.7 N.S
Heart	Mean ± S.E Probability	60 2.4	65 2.4 N.S	46 2.3 P < 0.01	58 2.2 N.S	59 2.3 N.S
Muscle	Mean ± S.E Probability	47.5 1.7	45.0 1.3 N.S	39.5 1.2 P < 0.01	48.1 1.7 N.S	42.5 1.6 N.S
Kidney	Mean ± S.E Probability	45.0 1.4	46.2 1.3 N.S	38 1.3 P < 0.01	47.1 1.2 N.S	40.1 1.3 N.S

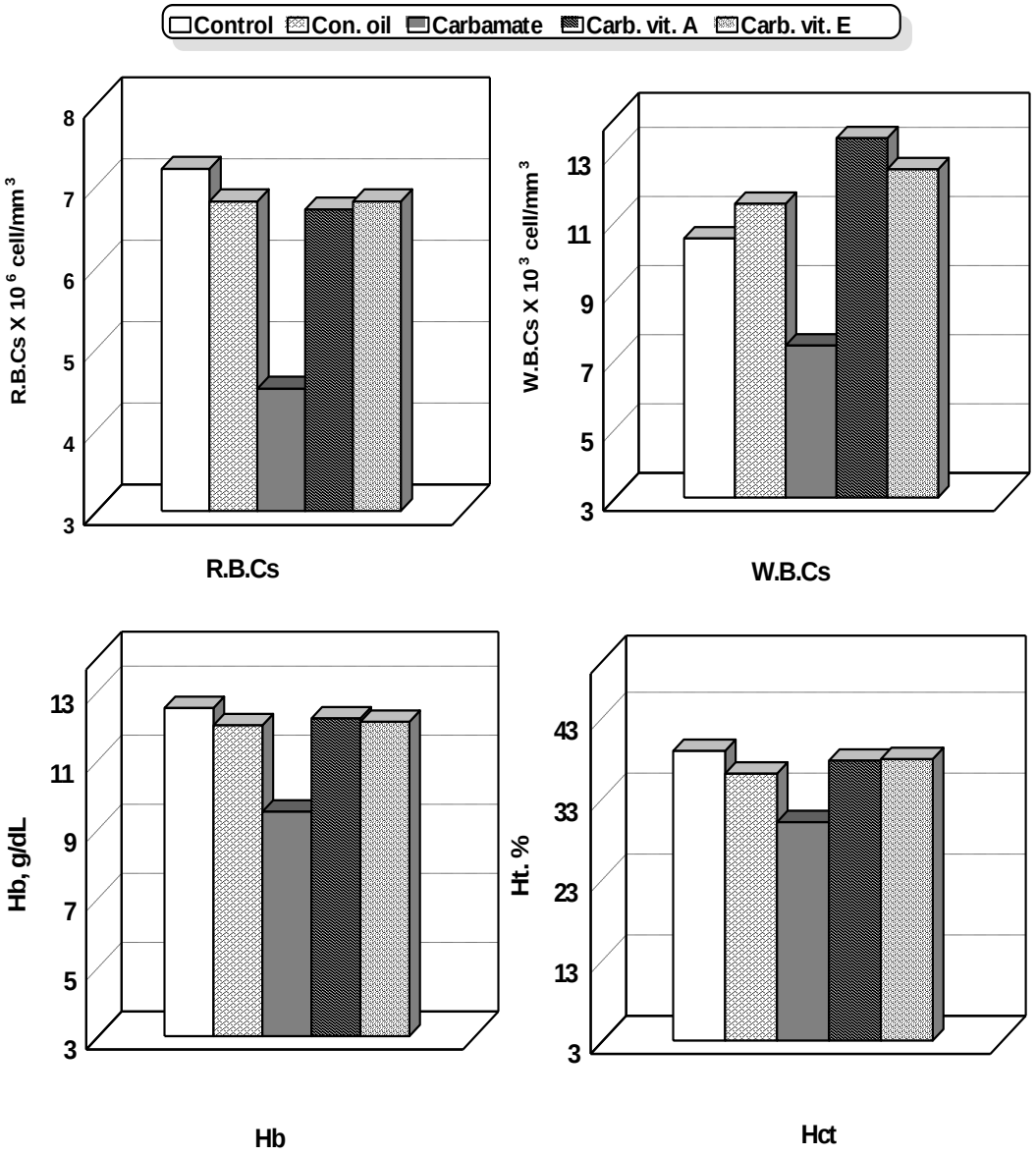


Fig.(1) Diagrammatic representations of some haematological parameters of male albino rats treated with oil, carbamate, vit A. and vit E

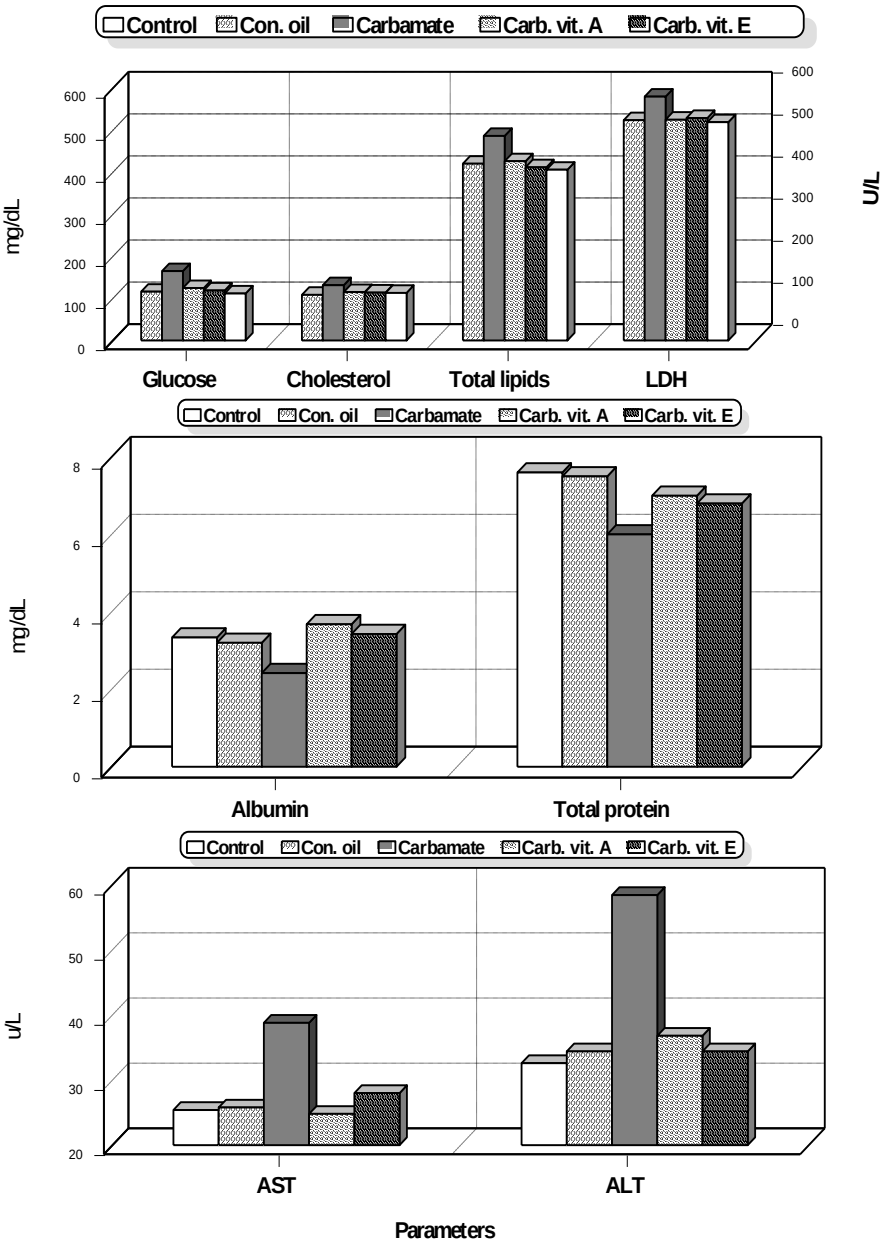


Fig.(2) Diagrammatic representations of some biochmecal parameters of male albino rats treated with oil, carbamate, vit.A and vit. E .

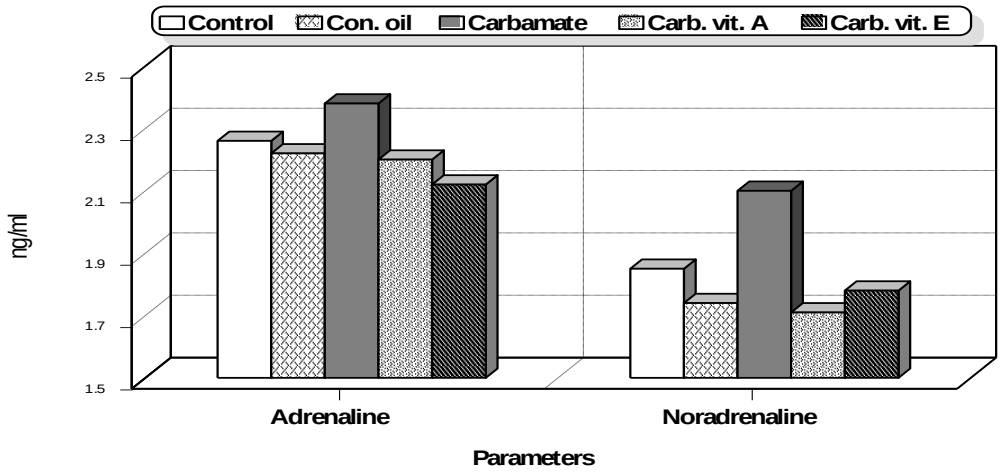
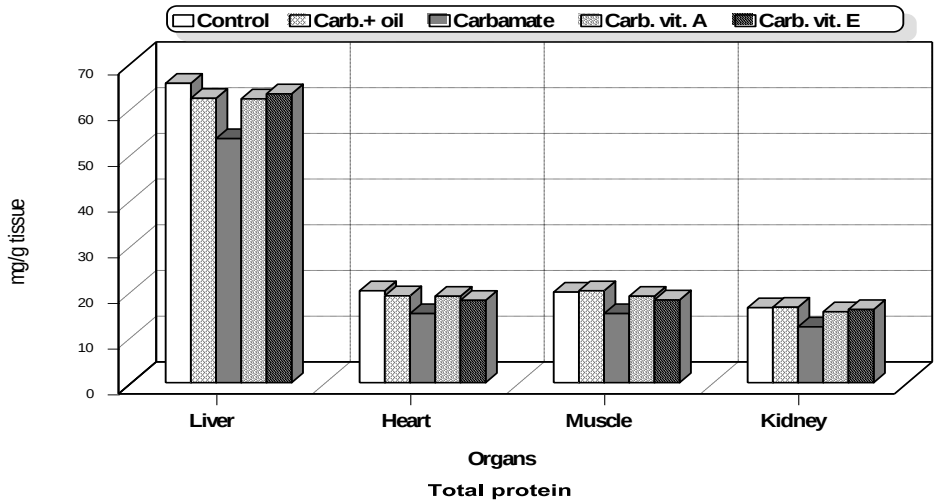


Fig.(3) Diagrammatic representations of adrenaline and noradrenaline of male albino rats treated with oil, carbamate, vit.A and vit. E .



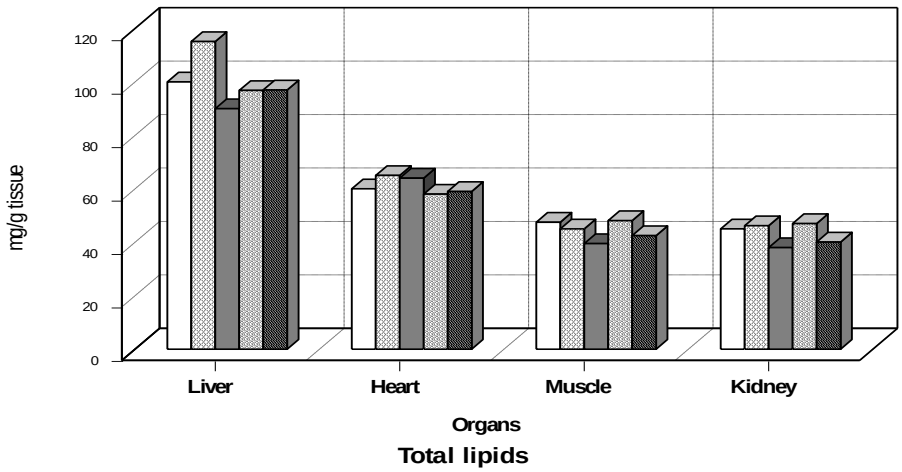


Fig.(4) Diagrammatic representations of total proteins and total lipides in some organs of male albino rats treated with oil, carbamate, vit.A and vit. E .

التسمم بالكرباميت والتأثير الفعال (الحام) لكل من فيامين أ و فيتامين هـ على بعض المظاهر البيوكيميائية للفئران البيضاء

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لقد درس التأثير اليومى لتعاطى الكربماميت ($^1/_{10}$ من نصف المادة المميتة) عن طريق الفم للفئران البيضاء لمدة 30 يوماً متتالية وقد تم تقسيم الفئران الذكور إلى خمس مجموعات كالتالى :

المجموعة الأولى (مجموعة ضابطة) و**المجموعة الثانية** (مجموعة ضابطة + زيت)، **المجموعة الثالثة** أخذت جرعة من الكرباميت وهى تكافىء 0.012 مجم/كجم من وزن الجسم) **المجموعة الرابعة** أخذت جرعة الكرباميت السابقة + 700 مجم/كجم من وزن الجسم) من فيتامين أ المضاد للأكسدة ، **المجموعة الخامسة** تعاطت نفس الجرعة من الكرباميت + 10مجم/كجم من وزن الجسم من فيتامين هـ المضاد للأكسدة.

وقد سجلت الأعراض السمية ومنها عدم الإتزان، إسهال، الهزال وتيبس الأطراف الخلفية للفئران. وقد أظهرت المعايير الدموية إنخفاض معنوى فى عدد كرات الدم الحمراء والخلايا الدموية البيضاء ونسبة تركيز الهيموجلوبين والهيماتوكريت فى المجموعات التى عوملت بالكرباميت وقد تحسنت هذه القياسات فى المجموعات التى عولجت بالفيتامينات المضادة للأكسدة. وقد تم قياس الدهون الكلية، الكوليسترول والبروتينات الكلية والألبيومين والجلوكوز وإنزيم اللاكتات النازع للهيدروجين LDH، الإنزيمات النازعة لمجموعة الأمين AST, ALT، الأدرينالين والنور أدريتالين فى مصل الدم. كما تم قياس البروتينات الكلية

والدهون الكلية لأنسجة الأعضاء التالية (الكبد ، القلب ، العضلات والكلى).

وقد أوضح هذا البحث أن الكروميت تسبب فى إرتفاع معنوى فى إنزيم اللاكتيت النازع للهيدروجين LDH والجلوكوز والدهون الفعلية والكوليسترول والإنزيمات الناقلة لمجموعة الأمين والإدريتالين والنور أدريتالين. ومن ناحية أخرى أوضحت النتائج إنخفاض معنوى فى البروتينات الكلية والألبومين لمصل الدم فى الفئران البيضاء.

وقد سجلت الدهون الكلية والبروتينات الكلية إنخفاض معنوى فى المجموعة التى عوملت بالكروميت فقط. ومن ناحية أخرى فإن المواد المضادة للأكسدة أظهرت تحسن ضد تأثير الكروميت على الأنسجة ولهذا فإنه من الواضح أن تعاطى فيتامين أ ، هـ تؤدى إلى إنخفاض تأثير الكروميت على التغيرات البيوكيميائية بقدر متنوع ومن خاصية المواد المانعة للأكسدة لكل من فيتامين أ ، هـ لإنها مسئولة عن الحماية الملحوظة ضد تسمم الكروميت.